REMARKS

Applicants have amended the specification to place the cross-reference to the related application section in the proper location as requested by the Examiner. Applicants respectfully request entry of this amendment and reconsideration of the application.

Withdrawn Rejection under 35 U.S.C. §112, First Paragraph: Written Description

Applicants note that the Examiner has withdrawn his written description rejection under 35 U.S.C. §112, first paragraph of claims 32-60.

Rejections Under 35 U.S.C. § 112, First Paragraph: Enablement

The Examiner rejected claims 32-61 under 35 U.S.C. §112, first paragraph for allegedly failing to comply with the enablement requirement. Applicants respectfully traverse this rejection.

The Examiner has the initial burden of presenting showing that the application does not teach how to make and use the invention. *In re Oetiker,* 977 F. 2d 1443 (Fed. Cir. 1992). Applicants respectfully submit that the Examiner has not met the burden.

The Examiner alleges that "said six examples do not provide adequate written description of the claimed method whereby one would be able to determine any and all single nucleotide polymorphisms in **any and all species of mammals**". (Office Action, page 5, emphasis added).

Applicants respectfully disagree with the Examiner's interpretation of the claims and point out that one of ordinary skill in the art would not interpret the claims in the manner that the Examiner does. Claims 32-61 include methods for identifying single nucleotide polymorphic sites in the genome of mammals of the **same species**, not different species. Further, claims 49-50, 52, 55 and 60 are specifically directed to horses and Claims 56-58 are specifically directed to horses of the same breed. Thus, the Examiner's interpretation of the claims is untenable.

Applicants respectfully submit that the specification fully enables the claims. In the specification the inventors teach the advantages of using SNPs as genetic markers over other types of polymorphisms including restriction fragment length polymorphisms (RFLPs), STRs (short tandem repeats), variable number tandem repeats (VNTRs). First, SNPs occur with greater allelic frequency and uniformity and thus can be linked to an individual trait (e.g., to identify an individual, parentage, etc.). Second, SNPs are more stable than other classes of polymorphism (e.g., VNTRs, STRs, RFLPs) and not subject to spontaneous mutation like other polymorphisms. Third, a SNP's allelic frequency can be inferred from a small number of representative samples. Fourth, SNPs allow a high degree of genetic information (e.g., base position and location) unlike other types of polymorphisms (see the specification at pages 13-15).

At page 37-45, and Examples 4 and 5 the inventors teach how SNPs can be used to determine, among other things, parentage and identity. Although, Examples 4 and 5 were conducted in horses, the same method can be conducted in mammals of the same species, and the specification clearly describes this, for example, at pages 4, lines 13-16, page 44 lines 29-36.

Applicants have also amended the claims to include that polymorphic sites comprises a SNP, and the polymorphic site is immediately flanked by a 3' and 5' invariant nucleotide sequence and that the polymorphic sites correspond to the same location of the genome. Thus, the method utilizes specific types of SNPs at the same corresponding location on the genome or locus. Moreover, Examples 1-5 alone utilize 18 polymorphic loci in sixty horses, over 1,000 SNPs utilized in the method. Applicants submit the specification provides fully enables the claims. The specification at pages 13-15, page 44, lines 29-36 and Examples 1-6 clearly discloses and enables conducting genetic analysis using SNPs from mammalian DNA of the same species.

The Examiner asserts that "of the six examples provided, none disclose how one would test and evaluate the myriad 'species of interest,' much less identify said single nucleotide polymorphisms in a simultaneous manner..." (Office Action, page 5). Applicants respectfully submit that the Examiner is using improper hindsight to interpret

the claims by requiring disclosure for simultaneous sequencing in the specification—a technology that was not invented until about 2002 (see Murphy Am. J. Pathology 2002 July; 16(1): 27-33), which is well after the filing date of the present application and one of ordinary skill in the art would not interpret the claims the way the Examiner is interpreting them--using improper hindsight.

As previously argued in the prior response, the Examiner's reliance on *Genentech v. Novo Nordisk* ("*Genentech*") as analogous to the present case is misplaced. *Genentech* was decided on strikingly different facts. In *Genentech*, the claims recited a method for making human growth hormone in a fusion protein and cleaving the fusion protein to make the growth hormone. The patentees in *Genentech* tried to rely on the level of skill in the art to enable the claim, but at the time of filing the application it was ***not*** known in the art how to cleave a fusion protein to make growth hormone, ***where the cleaving of the fusion protein was the novel aspect of the claim***. In contrast, the novel aspect of the amended claims does not include claims to individual SNPs, but methods using the combinations of SNPs as useful genetic markers. Thus, *Genentech* sheds no light on any alleged written description or enablement issues with respect to the present claims. *Genentech* is simply inapplicable to the facts of this case.

Moreover, claims 59 and 60 include that the starting material involves known SNPs to determine the parentage testing. It is respectfully submitted, that the starting material is clearly provided by the specification. Applicants submit that the specification fully complies with the enablement requirement for methods of identifying and characterizing single nucleotide polymorphic sites in the genome of mammals of the same species. Accordingly, Applicants respectfully request withdrawal of this rejection.

Rejections under 35 U.S.C. §103(a)

The Examiner rejects claims 32-36, 38-43, 45-46,48, 51, 53, 54, and 59 under 35 U.S.C. §103(a) as allegedly being obvious over *Eur. J. Immonogenet.* 18:33-55 (1991) (Erlich). The Examiner also rejects claims 33-35 and 39-55 under 35 U.S.C. §103(a) as

allegedly being obvious over Erlich in view of *Swiss Medical Weekly* 119:815-825 (1989) (Fey). Applicants respectfully traverse these rejections.

To establish a *prima facie* case of obviousness, all of the claim elements must be taught or suggested by the prior art. *In re Vaeck,* 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir.1991). Applicants respectfully disagree with the Examiner's position and submit that neither Erlich nor Fey alone or in combination disclose, teach or suggest methods of using a panel of SNPs to determine allelic frequency, parentage and identity among mammals of the same species.

In the Office Action, the Examiner alleges that Erlich shows a method of identifying SNPs in a genome of interest, particularly in 18 different sequences (Office Action, item 17 on page 11). The Examiner refers to Figure 1-3 and Table 1 of Erlich in support of his position. Applicants respectfully disagree with the Examiner.

Erlich teaches typing the HLA gene using allele specific oligonucleotide probes (ASO) that hybridize to HLA class II polymorphisms DQA1, DQB1, DRB1, and DPB1. These HLA class II polymorphisms are polymorphic regions and not single nucleotides polymorphisms. The allele specific probes listed in Table 1, which the Examiner refers to, do not discriminate among alleles that differ by a single nucleotide base. If the ASO probes did, they would differ by one nucleotide base as well. Figure 3, which the Examiner also refers to, illustrates the DNA sequence and probe alignments for the probes listed in Table 2. Note the DNA locus and probe alignments listed in Table 2 of Erlich and the regions he interrogates have multiple nucleotide variations and could not and are not considered single nucleotide polymorphisms that are immediately flanked by a 3' and 5' invariant nucleotide sequence as currently claimed.

In contrast to SNPs, Erlich teaches polymorphic regions containing at least 2 to 3 nucleotide variations:

> The allelic diversity at the DPB1 locus presents more of a challenge for oligonucleotide probe typing because of the dispersed nature of the **polymorphic sequences** (Fig. 3). The second exon contains six variable regions (A to F) with a limited number of **polymorphic**

> **residues (n=2-3) at each position** (Erlich, at page 37, emphasis added).

Erlich's ASO probes each are directed against a specific allele having a polymorphic region that is arrayed and exposed to PCR amplicons generated by the sample, and it is the pattern on the array that reveals the genotype:

> Our approach has been to use a panel of 15 oligonucleotide probes (listed in Table 2) specific for the sequence variants in four polymorphic regions with the pattern of probe hybridization identifying a specific DPB allele (see Table 3). (Erlich, at page 40).

Thus, it is the pattern of matching ASOs with sample amplicons, where the amplicons are of polymorphic regions, not SNPs that identifies genotypes. Accordingly, Erlich teaches trait association by polymorphic region, not by SNPs.

Fey, like Erlich, does not disclose, teach or suggest utilizing SNPs. Fey teaches two different types of polymorphisms: (1) RFLPs and (2) highly variable regions (HVRs)--which is a type of VNTR. These types of polymorphisms are discussed on pages 2 and 3 of the specification. And again, one of ordinary skill in the art would not consider these types of polymorphisms SNPs.

Moreover, Applicants submit that before the filing of the present application, one of ordinary skill in the art would not consider using a panel of SNPs as genetic markers and would not have recognized that SNPs could provide valuable genetic information including, among other things, determining allelic frequency, parentage and identity among mammals of the same species.

Because neither Erlich nor Fey disclose, teach or suggest methods of using a panel of SNPs to determine, among other things, allelic frequency, parentage and identity among mammals of the same species, Applicants respectfully submit that the present claims cannot be considered obvious. Accordingly, Applicants respectfully request withdrawal of the rejections.

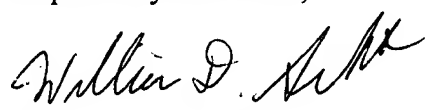
Conclusion

Reconsideration and allowance are respectfully solicited.

If any additional fees are due, or an overpayment has been made, please charge, or credit, our Deposit Account No. 11-0171 for such sum.

If the Examiner has any questions regarding the present application, the Examiner is cordially invited to contact Applicants' attorney at the telephone number provided below.

Respectfully submitted,



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